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# Agar: a novel, efficient, and biodegradable catalyst for the one-pot three-component and green synthesis of 2,3-dihydroquinazolin-4(1*H*)-one, 4*H*-pyrimidobenzothiazole and 2-aminobenzothiazolomethylnaphthol derivatives

**Ashraf Moradi · Reza Heydari · Malek Taher Maghsoodlou**

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**Abstract** 3-(2′-Benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)- one, 1-((benzo[d]thiazol-2-ylamino) (aryl)-methyl)naphthalen-2-ol and 4*H*-pyrimido[2,1-b][1,3]benzothiazoles derivatives were prepared via one-pot three-component reaction of arylaldehydes, 2-aminobenzothiazole and isatoic anhydride or *β*-naphthol or ethyl/methyl acetoacetate in the presence of agar as a highly efficient homogenous catalyst. The use of a non-toxic and biodegradable catalyst, as well as high yields, short reaction time, simple work-up and green conditions are the most important advantages of this method.

**Keywords** 3-(2′-Benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-ones · 1-((Benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol · 4*H*-pyrimido[2,1-b][1,3]benzothiazole · Agar · Green chemistry

## Introduction

The development of environmentally benign, efficient, and economical methods for the synthesis of biologically interesting compounds remains a significant challenge in synthetic chemistry [1, 2]. One-pot multi-component reaction strategies (MCRs) are believed to exhibit negative activation volumes owing to the condensation of several molecules into a single reactive intermediate and product because of their convergence, productivity, facile performance and high yields [3].

Dihydroquinazolin-4(1*H*)-ones constitute an important class of heterocyclic compounds that exhibit a wide spectrum of biological and physiological activities and pharmacological properties [4, 5], such as anticancer, antidiuretic, anticonvulsant, antibacterial, antifungal activity [6], and mono-amine oxidase inhibition, and

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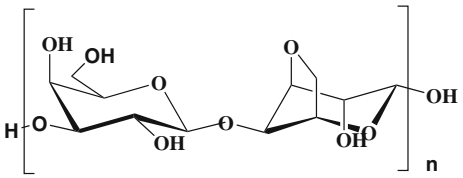


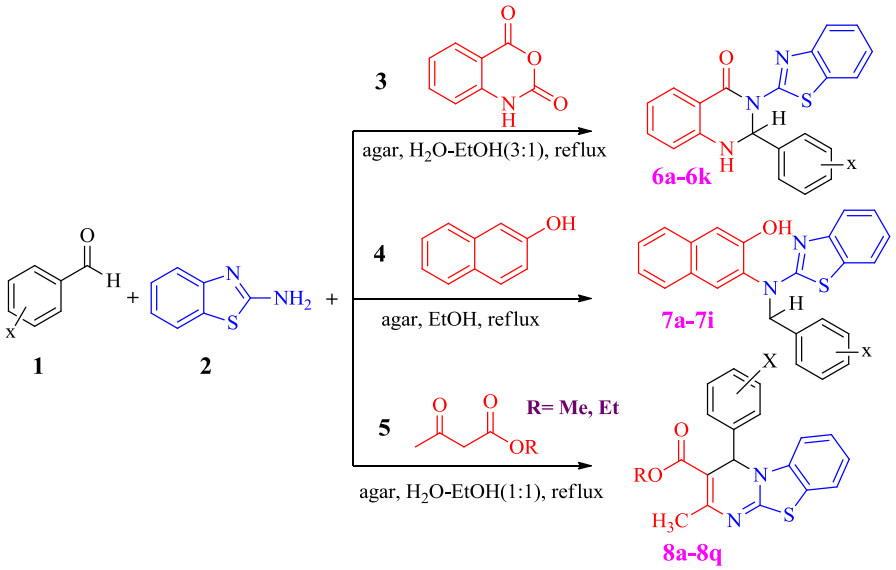

**Fig. 1** The structure of an agarose polymer

are also used as 5-hydroxytryptamine (5-HT) receptor ligands [7]. Recently, Lindsley and coworkers observed the metabotropic glutamate receptor (mGluR) properties of this class of compounds [8]. Thus, developing versatile approaches to the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones, 4*H*-pyrimido [2,1-b][1,3]benzothiazoles and 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ols still remains a highly desired goal in organic synthesis, because of their potential biological and pharmaceutical activities. There are many reports on the synthesis of dihydroquinazolin-4(1*H*)-ones, 4*H*-pyrimido [2,1-b][1,3]benzothiazole and 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol derivatives by three-component reaction of aldehydes, 2-aminobenzothiazole and isatoic anhydride or *β*-naphthol or ethyl/methyl acetoacetate in the presence of heterogeneous catalysts, for example $Fe_3O_4$ nanoparticles [9], copolymer-p-TSA [10], p-TSA–$NaHSO_3$ [11], silica sulfuric acid [12], gallium(III) triflate [13], Amberlyst-15 [14], KAl(SOO(alum) [12], montmorillonite K-10 [15], zinc(II) perfluorooctanoate [16], the ionic liquids 1-butyl-3-methylimidazolium bromide[bmim]Br or [bmim]PF6 [17, 18], $[Al(H_2PO_4)_3]$ [22], tetramethylguanidinium trifluoroacetate (TMGT) [19], silica sulfuric acid (SSA) [20], and sulfamic acid (SA) [21].

In recent years, the emphasis of science and technology has shifted more toward environmentally benign and sustainable resources and progress: in this regard, use of natural catalysts has received considerable attention in organic chemistry. In particular, natural biopolymers are important candidates to explore for catalysts, and their properties provide the possibility to perform reactions for acid-sensitive substrates, under milder reaction conditions and better selectivity [23–25, 33].

Agar is derived from the polysaccharide agarose, which forms the supporting structure in the cell walls of certain species of algae. These algae are known as agarophytes and belong to the Rhodophyta (red algae) phylum [27, 28]. Generally, agar is actually a mixture of components: the linear polysaccharide agarose, agarose polymer, sugars such as galactose, gluconic acid and xylose, and amino acids such as garyn, glutamic acid, threonine, and a heterogeneous mixture of smaller molecules called agaropectin [29]. In chemical terms, agar is a polymer made up of subunits of the sugar galactose (Fig. 1). This small natural product contains many hydroxyl groups and can therefore can act as a mild catalytic system [30].

During the course of our studies in developing efficient synthetic methodologies for the synthesis of substituted benzothiazole heterocyclic compounds, and our interest in multi-component reactions [31–33], we report a practical method in which commercially available agar acts as a bio-resource catalyst in synthesizing benzothiazoquinazoline, 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol and 4*H*-pyrimido [2,1-b][1,3]benzothiazole derivatives employing the one-pot three-component condensation reactions strategy of aldehyde **1** with




**Scheme 1** Synthesis of 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-one, 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol and 4*H*-pyrimido [2,1-b][1,3]benzothiazole derivatives in the presence of agar as the catalyst

2-aminobenzothiazole **2** and isatoic anhydride **3** or *β*-naphthol **4** or ethyl/methyl acetoacetate/acetacetate **5a**and **5b** under classical heating conditions (Scheme 1).

## Experimental

Materials and equipment's

All reagents were purchased from Merck, Fluka and Aldrich and used without further purification. The NMR spectra were recorded on a Bruker Avance DPX 300 MHz spectrometer using $CDCl_3$ or DMSO, as solvent. Chemical shifts have been expressed in (ppm) downfield from TMS. IR spectra were recorded on a JASCO FT-IR 460 plus spectrophotometer. Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. All the reactions are monitored by thin layer chromatography (TLC), which was performed on silica-gel Poly Gram SIL G/UV 254 plates.

General procedure for the synthesis of 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-one derivatives

A mixture of an aldehyde (1.0 mmol), 2-aminobenzothiazole (1.0 mmol), isatoic anhydride (1.0 mmol) and agar (0.15 g) in water–ethanol (3:1) was stirred under reflux condition. The progress of the reaction was monitored by TLC. After

completion of the reaction, the reaction mixture was cooled to room temperature, and diluted with water. The mixture was filtered and then washed with distilled water for separation of the product. The crude product was recrystallized from ethanol to afford the pure 3-(2′-benzothiazolyl)-2, 3-dihydroquinazolin-4(1*H*)-one derivatives. The desired pure products were characterized by comparison of their physicaldata (melting points, IR and $^1$H NMR) with those of known compounds in the literature [18, 26, 34, 35].

General procedure for the synthesis of 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol derivatives

A mixture of an aldehyde (1.0 mmol), 2-aminobenzothiazole (1.0 mmol), *β*-naphthol (1.0 mmol) and agar (0.1 g) was added to 4 mL of ethanol. Then, the reaction mixture was stirred under reflux condition for an appropriate time. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature, and diluted with water. The mixture was filtered and then washed with distilled water for separation of the product. The crude product was recrystallized from ethanol to afford the pure 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol derivatives. The desired pure products were characterized by comparison of their physical data (melting points, IR and $^1$H NMR) with those of known compounds in the literature [37–39].

General procedure for the synthesis of 4*H*-pyrimido [2,1-b][1,3]benzothiazoles

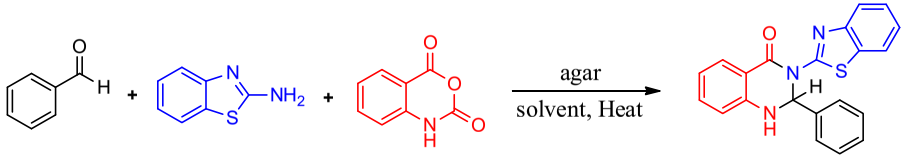
A mixture of an aldehyde (1.0 mmol), 2-aminobenzothiazole (1.0 mmol), ethyl/methyl acetoacetate (1.0 mmol) and agar (0.1 g) in water–ethanol (1:1), was stirred at reflux condition. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature, and diluted with water. The mixture was filtered, washed with distilled water for separation of the product. The crude product was recrystallized from ethanol to afford the pure 4*H*-pyrimido [2,1-b][1,3]benzothiazole derivatives. The desired pure products were characterized by comparison of their physical data (melting points, IR and $^1$H NMR) with those of known compounds in the literature [40–44].

Some spectral data for selected products are represented below

*3-(2′-Benzothiazolyl)-2,3-dihydro-2(4-nitrophenyl)-quinazolin-4(1H)-one (**6c**)*

m.p = 242–244 °C; IR (KBr, cm$^{-1}$): 3,375, 1,647, 1,613, 1,521; $^1$HNMR (300 MHz, DMSO-d$_6$): $\delta$ (ppm) = 6.81 (1*H*, *t*, 1CH), 7.00 (1*H*, *d*, 1CH), 7.34 (1*H*, *t*, 1CH), 7.41 (1*H*, *t*, 1CH), 7.44 (1*H*, *t*, 1CH), 7.57 (2*H*, *d*, 2CH), 7.67 (1*H*, *s*, 1CH), 7.77 (1*H*, *d*, 1CH), H7.81 (1*H*, *d*, 1CH), 8.05 (1*H*, *d*, 1CH), 8.15 (2*H*, *d*, 2CH), 8.46 (1*H*, *s*, 1NH).

**Table 1** Optimization conditions for preparation of 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-ones in the presence of different amounts of agar, temperature and solvent

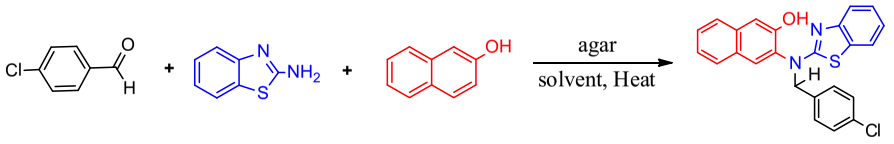



| Entry | Temperature (°C) | Solvent | Catalyst (g) | Time (min) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | r.t | EtOH | – | 24 h | Trace |
| 2 | Reflux | EtOH | – | 24 h | Trace |
| 3 | r.t | EtOH | 0.1 | 24 h | Trace |
| 4 | 50 | EtOH | 0.1 | 120 | 42 |
| 5 | Reflux | EtOH | 0.1 | 25 | 81 |
| 6 | 70 | MeOH | 0.1 | 25 | 75 |
| 7 | 90 | MeOH | 0.1 | 25 | 91 |
| 8 | Reflux | MeOH | 0.1 | 25 | 92 |
| 9 | 70 | $H_2O$-EtOH(1:1) | 0.1 | 45 | 68 |
| 10 | Reflux | $H_2O$-EtOH(1:1) | 0.1 | 35 | 85 |
| 11 | Reflux | $H_2O$-EtOH(1:3) | 0.1 | 35 | 83 |
| 12 | Reflux | $H_2O$-EtOH(3:1) | 0.1 | 30 | 87 |
| 13 | Reflux | $H_2O$-EtOH(3:1) | 0.05 | 30 | 82 |
| 14 | **Reflux** | $H_2O$-EtOH(3:1) | **0.15** | **25** | **94** |
| 15 | Reflux | $H_2O$-EtOH(3:1) | 0.2 | 25 | 91 |

The best result is highlighted in bold

[a] Yields refer to isolated pure product

**Table 2** Optimization conditions for preparation of 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-oles in the presence of different amounts of agar, temperature and solvent




| Entry | Temperature (°C) | Solvent | Catalyst (g) | Time (min) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | r.t | EtOH | 0.1 | 24 h | 27 |
| 2 | 50 | EtOH | 0.1 | 65 | 52 |
| **3** | **Reflux** | **EtOH** | **0.1** | **40** | **94** |
| 4 | 70 | MeOH | 0.1 | 40 | 86 |
| 5 | 90 | MeOH | 0.1 | 40 | 87 |
| 6 | Reflux | MeOH | 0.1 | 40 | 91 |
| 7 | Reflux | $H_2O$-EtOH(1:1) | 0.1 | 50 | 89 |
| 8 | Reflux | EtOH | 0.05 | 45 | 79 |
| 9 | Reflux | EtOH | 0.15 | 40 | 92 |

The best result is highlighted in bold

[a] Yields refer to isolated pure product

*3-(2′-Benzothiazolyl)-2,3-dihydro-2(4-cholorophenyl)-quinazolin-4(1H)-one (**6e**)*

m.p = 192–193 °C; IR (KBr, $cm^{-1}$): 3,334, 1,635, 1,609, 1,506, 1,405, 1,251; $^1$HNMR (300 MHz, DMSO-d): $\delta$ (ppm) = 6.81 (1*H*, *t*, 1CH), 6.96 (1*H*, *d*, 1CH), 7.30 (2*H*, *d*, 2CH), 7.36 (1*H*, *t*, 1CH), 7.38 (2*H*, *d*, 2CH), 7.42 (1*H*, *t*, 1CH), 7.46 (1*H*, *t*, 1CH),7.54 (1*H*, *d*, 1CH($sp^3$)), 7.78 (1*H*, *d*, 1CH), 7.79 (1*H*, *d*, 1CH),8.06 (1*H*, *d*, 1CH), 8.34 (1*H*, NH).

*3-(2′-Benzothiazolyl)-2,3-dihydro-2(4-methylphenyl)-quinazolin-4(1H)-one (**6i**)*

m.p = 198–199 °C; IR (KBr, $cm^{-1}$): 3,342, 1,630, 1,612, 1,503, 1,432, 1,251; $^1$HNMR (300 MHz, DMSO-d6): $\delta$ (ppm) = 2.17 (3*H*, *s*, $CH_3$), 6.78 (1*H*, *t*, CH), 6.93 (1*H*, *d*, CH), 7.08 (2*H*, *d*, 2CH), 7.17 (2*H*, *d*, 2CH), 7.35 (1*H*, *t*, CH),7.38(1*H*, *t*, CH), 7.45 (1*H*, *t*, CH), 7.51(1*H*, *d*, CH($sp^3$)), 7.77 (1*H*, *t*, CH), 7.79 (1*H*, *d*, CH), 8.04 (1*H*, *d*, CH), 8.30 (1*H*, *d*, NH).

*3-(2′-Benzothiazolyl)-2,3-dihydro-2(4-methoxyphenyl)-quinazolin-4(1H)-one (**6k**)*

m.p = 183–185 °C; IR (KBr, $cm^{-1}$): 3,347, 1,635, 1,608, 1,508, 1,433, 1,304, 1,230; $^1$HNMR (300 MHz, DMSO-d6): $\delta$ (ppm) = 3.63 (3*H*, *s*, OCH3), 6.78 (1*H*, *t*, CH), 6.83 (2*H*, *d*, 2CH), 6.94 (1*H*, *d*, CH),7.21 (2*H*, *d*, 2CH), 7.34 (1*H*, *t*, CH), 7.39 (1*H*, *t*, CH), 7.44(1*H*, *t*, CH), 7.52 (1*H*, br *s*, CH($sp^3$)), 7.78(1*H*, *d*, CH), 7.81 (1*H*, *d*, CH), 8.04 (1*H*, *d*, CH), 8.32 (1*H*, br *s*, NH).

*1-((Benzo[d]thiazol-2-ylamino)(4-chloro-phenyl)methyl)naphthalen-2-ol (**7e**)*

m.p = 209–210 °C; IR (KBr, $cm^{-1}$): 3,383, 1,604, 1,568, 1,503, 1,450 $cm^{-1}$; $^1$HNMR (300 MHz, DMSO-$d_6$): $\delta$ (ppm) = 6.99–7.82 (*m*, 15*H*, 14$H_{arom}$ and CH-NH), 8.82 (*s*, 1*H*, NH), 10.19 (*s*, 1*H*, OH).

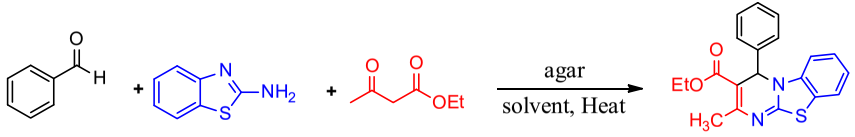
*1-((Benzo[d]thiazol-2-ylamino)(4-methoxy-phenyl)methyl)naphthalen-2-ol (**7k**)*

m.p = 175–176 °C; IR (KBr, $cm^{-1}$): 3,366, 1,589, 1,546, 1,509, 1,451 $cm^{-1}$; $^1$HNMR (300 MHz, DMSO-$d_6$): $\delta$ (ppm) = 3.68 (*s*, 3*H*, $OCH_3$), 6.82–7.81 (*m*, 15*H*, 14$H_{arom}$ and CH–NH), 8.78 (*s*, 1*H*, NH), 10.14 (*s*, 1*H*, OH).

*2-Methyl-4-(2-chlorophenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylic acid methyl ester (**8c**)*

m.p = 128–129 °C. IR (KBr, $cm^{-1}$): 2,935, 1,680, 1,596, 1,516, 1,383, 1,182, 974, 827, 690 $cm^{-1}$; $^1$HNMR (300 MHz, $CDCl_3$): $\delta$ (ppm) = 1.24 (*t*, 3*H*, $CH_3$), 2.44 (*s*, 3*H*, $CH_3$), 4.15 (*q*, 2*H*, $OCH_2$), 6.74 (*s*, 1*H*, CH), 7.08–7.16 (*m*, 2*H*, Ar–H), 7.19–7.28 (*m*, 2*H*, Ar–H), 7.39 (*d*, 1*H*, Ar–H), 7.46 (*d*, 2*H*, Ar–H), 7.62 (*d*, 1*H*, Ar–H).

**Table 3** Optimization conditions for preparation of 4*H*-pyrimido [2,1-b][1,3]benzothiazoles in the presence of different amounts of agar, temperature and solvent




| Entry | Temperature (°C) | Solvent | Catalyst (g) | Time (min) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | r.t | EtOH | 0.1 | 24 h | trace |
| 2 | 50 | EtOH | 0.1 | 120 | 68 |
| 3 | Reflux | EtOH | 0.1 | 40 | 83 |
| 4 | Reflux | MeOH | 0.1 | 50 | 92 |
| 5 | 70 | $H_2O$-EtOH(1:1) | 0.1 | 55 | 73 |
| **6** | **Reflux** | **$H_2O$-EtOH(1:1)** | **0.1** | **45** | **92** |
| 7 | Reflux | $H_2O$-EtOH(1:3) | 0.1 | 50 | 91 |
| 8 | Reflux | $H_2O$-EtOH(3:1) | 0.1 | 50 | 82 |
| 9 | Reflux | $H_2O$-EtOH(1:1) | 0.05 | 55 | 86 |
| 10 | Reflux | $H_2O$-EtOH(1:1) | 0.15 | 45 | 91 |

The best result is highlighted in bold

[a] Yields refer to isolated pure product

**Table 4** Preparation of 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)- one, 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol and 4*H*-pyrimido [2,1-b][1,3]benzothiazole derivatives in the presence of agar as biodegradable catalyst in green solvent under reflux condition

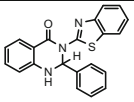
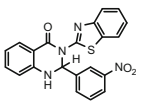
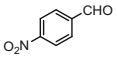
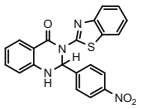
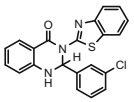
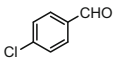
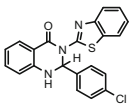
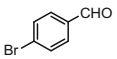
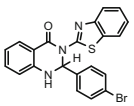
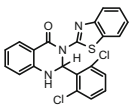
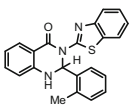
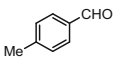
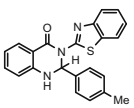
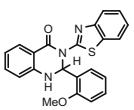
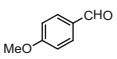
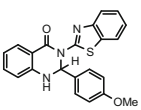
| Entry | Aldehyde | Substrate | | Product | Time(min) | Yield(%)[a] | m.p(°C)/Lit. m.p [Ref] |
|---|---|---|---|---|---|---|---|
| 1 |  |  | **6a** |  | 25 | 94 | 233-235/(234-236) [18] |
| 2 |  |  | **6b** |  | 20 | 95 | 252-253/(251-253) [18] |
| 3 |  |  | **6c** |  | 20 | 96 | 241-244/(242-244) [34] |
| 4 |  |  | **6d** |  | 20 | 91 | 160-163/(162-163) [34] |
| 5 |  |  | **6e** |  | 25 | 94 | 193-195/(192-193) [18] |
| 6 |  |  | **6f** |  | 25 | 91 | 231-233/(231-234) [18] |
| 7 |  |  | **6g** |  | 20 | 93 | 232-235/(229-239) [26] |
| 8 |  |  | **6h** |  | 45 | 90 | 200-203/(200-202) [18] |
| 9 |  |  | **6i** |  | 35 | 89 | 197-198/(198-199) [18] |
| 10 |  |  | **6j** |  | 40 | 90 | 225-228/(227-228) [36] |
| 11 |  |  | **6k** |  | 45 | 88 | 184-187/(183-185) [18] |

**Table 4** continued

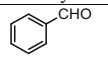
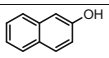
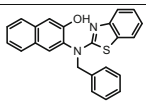
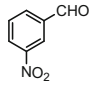
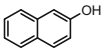
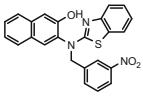
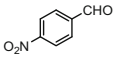
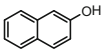
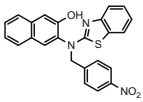
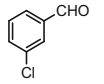
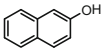
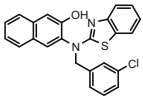
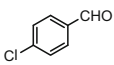
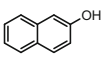
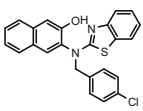
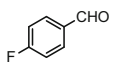
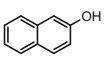
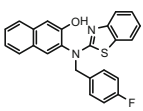
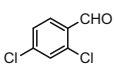
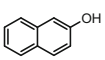
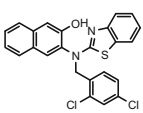
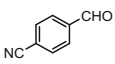
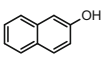
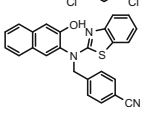
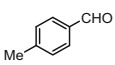
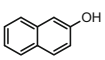
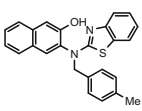
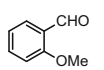
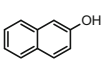
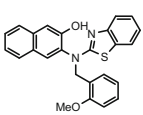
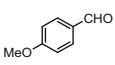
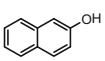
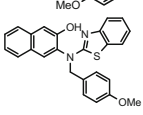
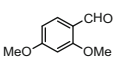
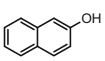
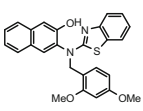
| Entry | Aldehyde | Substrate | Product | Time(min) | Yield(%)[a] | m.p(°C)/Lit. m.p [Ref] |
|---|---|---|---|---|---|---|
| 12 |  |  **7a** |  | 40 | 93 | 204-206/(202-203) [37] |
| 13 |  |  **7b** |  | 30 | 95 | 197-200/(198-199) [38] |
| 14 |  |  **7c** |  | 35 | 95 | 187-191/(190-191) [37] |
| 15 |  |  **7d** |  | 45 | 90 | 191-192/(192-194) [39] |
| 16 |  |  **7e** |  | 40 | 94 | 209-213/(209-210) [37] |
| 17 |  |  **7f** |  | 50 | 91 | 186-188/(188-189) [37] |
| 18 |  |  **7g** |  | 50 | 88 | 207-208/(206-207) [37] |
| 19 |  |  **7h** |  | 30 | 95 | 216-218/(214-215) [36] |
| 20 |  |  **7i** |  | 65 | 91 | 182-184/(182-183) [38] |
| 21 |  |  **7j** |  | 75 | 88 | 166-169/(165-167) [39] |
| 22 |  |  **7k** |  | 60 | 91 | 172-174/(175-176) [39] |
| 23 |  |  **7l** |  | 80 | 87 | 160-162/(161-163) [39] |

**Table 4** continued

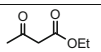
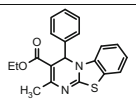
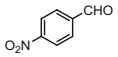
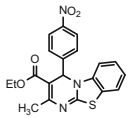
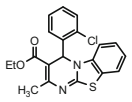
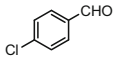
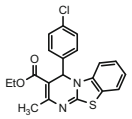
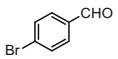
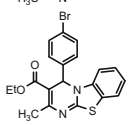
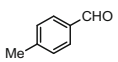
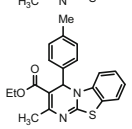
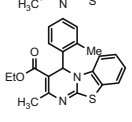
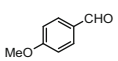
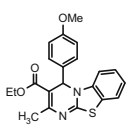
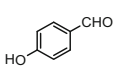
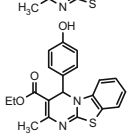
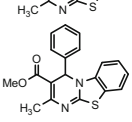
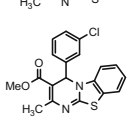
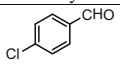
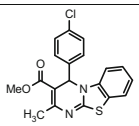
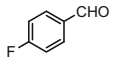
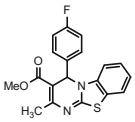
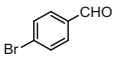
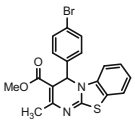
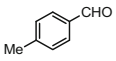
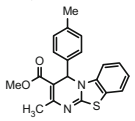
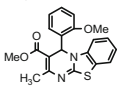
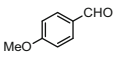
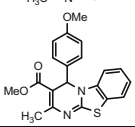
| Entry | Aldehyde | Substrate | | Product | Time(min) | Yield(%)[a] | m.p(°C)/Lit. m.p [Ref] |
|---|---|---|---|---|---|---|---|
| 24 |  |  | **8a** |  | 45 | 92 | 170-174/173-175 [40] |
| 25 |  |  | **8b** |  | 70 | 91 | 154-157/156-158 [40] |
| 26 |  |  | **8c** |  | 65 | 93 | 128-129/125-127 [43] |
| 27 |  |  | **8d** |  | 60 | 92 | 140/142-143 [42] |
| 28 |  |  | **8e** |  | 65 | 94 | 115-116/112-114 [40] |
| 29 |  |  | **8f** |  | 80 | 94 | 150-152/153-154 [42] |
| 30 |  |  | **8g** |  | 100 | 87 | 138-141/140-141 [40] |
| 31 |  |  | **8h** |  | 115 | 83 | 192-194/(194-196) [41] |
| 32 |  |  | **8i** |  | 110 | 89 | 213-214/209-210 [44] |
| 33 |  |  | **8j** |  | 40 | 90 | 142-145/144-145 [40] |
| 34 |  |  | **8k** |  | 50 | 93 | 142-143/139-140 [42] |

**Table 4** continued

| Entry | Aldehyde | Substrate | | Product | Time(min) | Yield(%)[a] | m.p(°C)/Lit. m.p [Ref] |
|---|---|---|---|---|---|---|---|
| 35 |  |  | **8l** |  | 50 | 96 | 176-178/179-180 [42] |
| 36 |  |  | **8m** |  | 135 | 89 | 158-162/160-161 [42] |
| 37 |  |  | **8n** |  | 60 | 95 | 167/166-167 [42] |
| 38 |  |  | **8o** |  | 70 | 90 | 153-156/154-155 [42] |
| 39 |  |  | **8p** |  | 120 | 87 | 142/145-146 [42] |
| 40 |  |  | **8q** |  | 110 | 84 | 148-151/150-153 [40] |

[a] Yields refer to isolated pure product

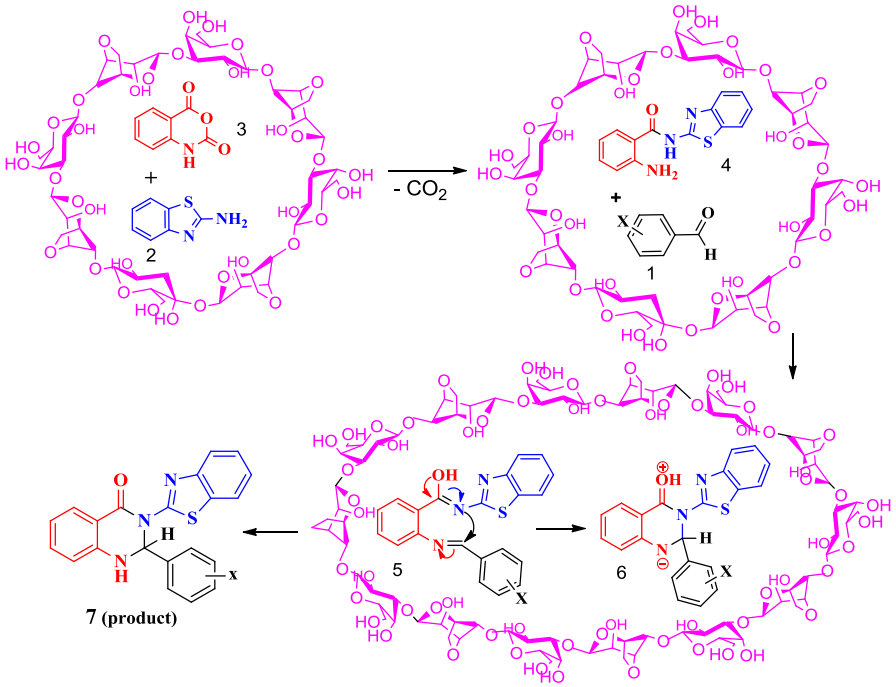
## Results and discussion

In preliminary experiments, the model reaction of aldehyde, 2-aminobenzothiazole, isatoic anhydride (molar ratio: 1:1:1) in EtOH was studied to establish the optimal conditions in the presence of different amounts of the catalyst at different temperature under thermal conditions. The results are summarized in Table 1. In the absence of a catalyst, only a trace amount of the desired product **6a** was obtained, even after long reaction time and refluxing (Table 1, entries 1, 2). The reaction was also examined in solvents such as EtOH, MeOH and $H_2O$-EtOH under similar conditions. The best result was obtained with $H_2O$-EtOH (3:1) (Table 1, entry 12). To determine the appropriate amount of catalyst, the model reaction was investigated with different quantities of agar, such as 0.05, 0.1, 0.15, 0.2 g. The results indicate that 0.15 g of agar is enough to carry out the reaction efficiently (Table 1, entry 14). Increasing the amount of agar neither improved the yield nor reaction time. As shown from Table 1, the best results used 0.15 g of the catalyst in $H_2O$-EtOH (3:1) under reflux condition (Table 1, entry 14).

This review was conducted for the preparation of 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol derivatives of 4-Chlorobenzaldehyde (1.0 mmol), 2-aminobenzothiazole (1.0 mmol) and $\beta$-naphthol (1.0 mmol) in the presence of 0.1 g of agar. It was found that the best results were obtained at reflux condition with 0.1 g of agar in ethanol (1:1) (Table 2, entry 3). We also tested for the preparation of 4*H*-pyrimido [2,1-b][1,3]benzothiazole derivatives by three-component condensation reaction of benzaldehyde (1.0 mmol), 2-aminobenzothiazole (1.0 mmol) and ethyl acetoacetate (1.0 mmol) in the presence of 0.1 g of agar in ethanol, water–ethanol, and methanol (Table 3). It was found that the best results were obtained at reflux condition with 0.1 g of agar in water–ethanol (1:1) (Table 3, entry 6). The results are summarized in Tables 2 and 3.

Using these optimized reaction, the scope and efficiency of the reaction were explored for the synthesis of a wide variety of substituted 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)- one, 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol and 4*H*-pyrimido [2,1-b][1,3]benzothiazoles using aldehydes, 2-aminobenzothiazole, isatoic anhydride or $\beta$-naphthol or ethyl/methyl acetoacetate. The results are summarized in Table 4.

We have not established a mechanism for the formation of 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)- ones ring systems, but a reasonable possibility for this synthesis in the presence of agar as catalyst is indicated in Scheme 2. We have




**Scheme 2** A plausible mechanism for the formation of 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-one in the presence of agar in water–etahanol under reflux condition

demonstrated that agar forms some kind of micelle-like structures, which can hold molecules and further catalyze reactions possibly activated by hydrogen bonds [23–25, 33]. The free OH groups in agarose distributed on the surface of the agarose activate the carbonyl group. The first step, condensation of 2-aminobenzothiazole **2** and isatoic anhydride **3**, produced intermediate **4** with the removal of $CO_2$ molecules. Then, activated aldehyde **1** was reacted with this intermediate **4** through an imine intermediate **5** synthesis. In the next step, intermediate **6** could be prepared by intermolecular nucleophilic attack of the amide nitrogen on activated imine carbon, cyclisation, 1,5-proton transfer and tautomerization, affording the corresponding product (Scheme 2).

## Conclusions

In conclusion, we have described a new simple biopolymer catalytic system, and a simple and efficient method for one-pot three-component synthesis of functionalized 3-(2′-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)- one, 1-((benzo[d]thiazol-2-ylamino)(aryl)-methyl)naphthalen-2-ol and 4*H*-pyrimido [2,1-b][1,3]benzothiazoles using aromatic aldehydes, 2-aminobenzothiazole, isatoic anhydride or ethyl/methyl acetoacetate or $\beta$-naphthol in the presence of agar as a highly effective and biodegradable green catalyst in ethanol or water–ethanol as a green solvent under reflux condition.

The present protocol has several significant advantages such as effectiveness, natural, biodegradable, clean, safe, non-toxic, environmentally friendly, inexpensive, easy-to-handle catalyst, green conditions, high yields, short reaction times, clean reaction conditions, simple work-up procedure, easy isolation of products, and mild reaction conditions, which together make a useful and an instrumental alternative to the existing methodologies. This work was performed for the first time.

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